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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,506	01/12/2001	Charlotte Kensil	106941.190	2171

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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 10/23/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/760,506

Applicant(s)

KENSIL, CHARLOTTE

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 31-41 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 31-41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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### **DETAILED ACTION**

Claims 31-41 are pending in the application.

#### ***Election/Restrictions***

Applicant's election without traverse of Group II (31-41) in Paper No. 13 is acknowledged.

Claims 1-31, 42 and 43 are cancelled. Accordingly, claims 31-41 are under examination.

#### ***Drawings***

The drawings are objected to because of the informalities as indicated by Draftsperson on PTO form 948 (see attached form). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. Any response to this office action which does not response to the above objections will be considered non-responsive.

#### ***Claim Objections***

Claim 40 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 32, the parent claim of claim 40, is drawn to a method of stimulating innate immune response comprising administering to an individual a saponin isolated from *Quillaja saponaria*. Claim 40 recites said method further enhances a natural killer cell response. A natural killer cell response is considered to be an innate immune response. Therefore, claim 40 fails to further limit the parent claim.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: “*specification* shall contain a written description of the invention. . in full, clear concise and exact terms...” The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that “as of the filing date sought, [the inventor] was in possession of the invention.” See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in “possession” of the invention claimed by describing the invention with all of its claimed limitations “by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention.” See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Claim 31 is drawn to a method of stimulating an innate immune response comprising administering an effective amount of a composition comprising a saponin. The specification defines the term “saponin” includes glycosidic triterpenoid compounds which produce foam in aqueous solution. The term also encompasses biologically active fragments and chemically

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modified saponins (see page 7, lines 15-20). However, the specification only teaches Q21 and Q7 saponin, isolated from Quillaja saponaria and purified by HPLC, stimulate natural killer cell activity in mouse. The specification fails to teach any other saponin, for example, saponin isolated from other plants, biological active fragments, or chemically modified saponin that is capable of enhance natural killer cell activity in mouse. Kensil (6,231,859) teaches that Quillaja saponins are structurally distinct from the saponins derived from other plant species (see col. 2, lines 21-26). In the absence of disclosure of a specific structure-function correlation, whether other saponins can elicit innate immune response is unpredictable. The specification fails to teach the structural-function relationship between the saponin and the innate immune response. Therefore, the specification fails to describe the invention in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

Claims 31-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of stimulating an innate immune response in a mouse by administering saponin isolated from Quillaja saponaria, does not reasonably provide enablement for a method of stimulating an innate immune response in any individual by administering any Quillaja saponaria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The nature of the invention is a method of stimulating innate immune response in an individual by administering a saponin to said individual. The specification discloses that

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administering QS21 and QS7 saponin enhances natural killer cell activity in a mouse and further protect said mouse from infection of *Listeria Monocytogenes*.

The state of art at the time of filing teaches that saponins isolated from Quillaja are structurally distinct from the saponins isolated from other plants. Two structural features that distinguish Quillaja saponaria saponins from those of other plants are a fatty acid domain and a triterpene aldehyde at carbon 4 of the triterpene (6,231,859, col.2, lines 21-33). QS7, QS17, QS18 or QS21 are HPLC and low pressure silica chromatography purified saponin from Quillaja (col.1, lines 55-60).

The breath of the claims is very broad. The broadest claim encompasses a method of stimulating an innate immune response in any individual by administering any saponin. The specification defines the term “saponin” includes glycosidic triterpenoid compounds which produce foam in aqueous solution. The term also encompasses biologically active fragments and chemically modified saponins (see page 7, lines 15-20). However, the teaching of the specification is limited. The specification only teaches a method of stimulate an innate immune response in a mouse by using saponins isolated from Quillaja. The specification fails to teach whether other saponins, for example, a saponin isolated from other plants, can stimulate innate immune response in an individual. The state of art teaches that other saponins are structurally distinct from Quillaja saponins. As such, whether other saponins would achieve the same effect as Quillaja saponins in stimulating an innate immune response is unpredictable. The specification also fails to teach the effective amount of Quillaja saponins that will stimulate innate immune response in an individual other than a mouse. Therefore, one skilled in the art

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would have to engage in undue amount of experimentation to determine how to practice the method commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 32-41, the word “derived” renders the claims indefinite because the nature and number of derivative process is unknown.

Regarding claims 33, the recitation of “wherein the saponin is modified” renders the claim indefinite because the nature of the modification is unknown. In other words, is the saponin chemically modified, purified from a plant, dissolved in a solvent, or simply mixed in a pharmaceutical carrier?

Regarding claim 41, the recitation “further enhances a natural killer cell response in a positive synergistic manner” renders the claim indefinite. In order for the saponin to enhance a natural killer cell response in a synergistic manner, there must be at least one more stimulant (besides saponin) to elicit a natural killer cell response first. However, the claim does not recite any other stimulant(s). Therefore, it is unclear how synergy will be determined.

Claims 31-41 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP

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§ 2172.01. The omitted steps are: How to determine whether an innate immune response is stimulated in said individual.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31-34, 37, 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Chavali et al. (1987, Immunobiol., Vol 174, pages 347-359).

The claims are drawn to a method of stimulating innate immune response comprising administering an effective amount of a composition comprising a saponin to an individual, wherein the individual can be either human or non-human mammal. The claims are further drawn to said method using saponin that is isolated from Quillaja saponaria and is substantially pure.

Chavali et al. disclose that the saponin isolated from Quillaja saponaria (see page 348, 4<sup>th</sup> paragraph, line 1) enhanced natural killer cell activity in mice, and such enhancement persisted for an extended period of time (see abstract, page 355, Table 7, page 356, 1<sup>st</sup> paragraph).

Therefore, the invention is anticipated by Chavali et al.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person



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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chavali et al., in view of Kensil (6,231,859).

The claims are drawn to a method of stimulate an innate immune response by administering QS7, QS17, QS18 or QS21 saponin to an individual.

The teaching of Chavali et al. is discussed above. However, Chavali et al. do not teach a method of stimulate innate immune response by using QS7, QS17, QS18 or QS21 saponin.

Kensil teaches that QS7, QS17, QS18 or QS21 are HPLC and low pressure silica chromatography purified saponin from Quillaja (col.1, lines 55-60). They have all been found to have excellent stimulatory effect on antibody response to soluble T-dependent protein antigens (see col. 2, lines 35-37), whereas QS7 and QS21 have the least toxicity.

It would have been obvious to one of ordinary skill in the art to use QS7, QS17, QS18 or QS21 saponin to stimulate innate immune response in an individual because of the combined teaching of Chavali et al., who taught saponin purified from Quillaja can stimulate natural killer cell response in mice, and Kensil, who teach that QS7, QS17, QS18 or QS21 is purified saponin from Quillaja. The ordinary artisan would have been motivated to do so because these saponins are structurally same as the saponin used in the Chavali reference and has low toxicity. Absent evidence from the contrary, the ordinary artisan would have reasonable expectation of success because the teaching of Chavali et al. have demonstrated that Quillaja saponin can stimulate natural killer cell activity. Therefore, the invention would have been obvious to one of ordinary skill in the art at the time the invention was made.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.  
October 20, 2002



**JAMES KETTER**  
**PRIMARY EXAMINER**